Medical Drug Clinical Criteria

Subject:	Revcovi (elapegademase-lvlr)		
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Overview

This document addresses the use of enzyme replacement therapy for adenosine deaminase deficiency. This inherited disease results in absence of functional adenosine deaminase (ADA), an enzyme responsible for the metabolism of adenosine substrates. Increased concentration of these substrates can lead to adverse effects in various organ systems, most notably the immune system. ADA deficiency typically leads to a severe combined immunodeficiency (SCID) with dysfunction of T-, B-, and natural killer (NK) cells that presents in the first few months of life. Diagnosis can be made by newborn screening, genetic testing, or assessment of laboratory results. Hallmark laboratory findings include absent or very low ADA activity in lysed erythrocytes or dried blood spots and a marked increase in deoxyadenosine triphosphate (dATP) levels in erythrocytes (also measured as dAXP). ADA deficiency would also lead to a significant decrease in ATP concentration in erythrocytes, absent or extremely low levels of s-adenosylhomocysteine hydrolase in erythrocytes, and increase in adenosine and 2'-deoxyadenosine in urine, plasma, and dried blood spots.

Treatment for ADA-SCID involves enzyme replacement therapy (ERT) and definitive treatment with hematopoietic stem cell transplantation (HSCT) or enrollment in gene therapy studies. Gene therapy for ADA-SCID remains investigational in the US. HSCT is the definitive treatment of choice that is most widely available. The most successful transplants occur with matched sibling and matched family donors (MSD/MFD). According to consensus-based guidelines (Grunebaum 2023), all patients should receive ERT (i.e. Revcovi) after diagnosis, followed by definitive treatment with MSD/MFD HSCT (or possibly gene therapy). If clinically stable, some patients may proceed immediately to MSD/MFD HSCT if available at diagnosis. Otherwise, ERT can be used as a "bridge" for relatively short periods (up to a few years) in most patients before undergoing HSCT (or gene therapy, if available). If definitive treatment is not available or has failed, ERT can be continued or reinstituted.

Adagen (pegademase bovine) was the first ERT approved by the FDA and is no longer commercially available. It was derived from bovine tissue and posed challenges for reliable and consistent production. Revcovi (elapegademase-lvlr) is a recombinant adenosine deaminase based on the bovine amino acid sequence. Revcovi successfully replaces the deficient ADA to provide consistent and stable ADA activity. As it is administered intramuscularly, it should not be used in patients with severe thrombocytopenia. Close clinical monitoring is important for all patients receiving ERT, especially if it is continued long term. Declining immunity may occur with continued use due to underlying disease mechanisms, poor compliance and/or the development of neutralizing antibodies to the drug.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Revcovi (elapegademase-lvlr)

Initial requests for Revcovi (elapegademase-lvlr)] may be approved if the following criteria are met:

I. Individual has a diagnosis of adenosine deaminase deficient severe combined immunodeficiency (ADA-SCID); AND

II. Documentation is provided that diagnosis is demonstrated by any of the following:
   A. Genetic testing revealing biallelic mutations in the ADA1 gene; **OR**
   B. Positive newborn screening via T cell receptor excision circles (TRECs); **OR**
   C. Characteristic laboratory findings including but not limited to decreased or absent ADA activity and increase in erythrocyte deoxyadenosine nucleotide (dATP/dAXP) levels;

AND

III. Revcovi (elapegademase-lvlr) will be used only until definitive therapy with hematopoietic stem cell transplantation (HSCT); **OR**
IV. Individual is not a suitable candidate for HSCT (including but not limited to matched sibling or family donor not available); **OR**
V. Individual has failed HSCT (~~Label; Kohn 2019~~Grunebaum 2023).

Continuation requests for Revcovi (elapegademase-lvlr)] may be approved for the following:

I. There is clinically significant improvement or stabilization in clinical signs and symptoms of the disease (Including but not limited to improved or stabilized plasma ADA activity, dAXP levels, total lymphocyte counts, and/or immune function).

Requests for Revcovi (elapegademase-lvlr)] may not be approved for the following:

I. Individual has severe thrombocytopenia; OR
II. When the above criteria are not met and for all other indications.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J3590	Unclassified biologics (When specified as [Revcovi] (elapegademase-lvlr))
C9399	Unclassified drugs or biologicals (When specified as [Revcovi] (elapegademase-lvlr)) (Hospital Outpatient Use ONLY)

ICD-10 Diagnosis

	All diagnoses pend

Document History

Revised: 03/11/2024
Document History:

- 03/11/2024 – Annual Review: Update references. Coding Reviewed: No changes.
- 04/04/2023 – Add new clinical criteria document for Revcovi. Coding Reviewed: Added HCPCS J3590, C9399. All diagnoses pend.

References

1. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: March 5, 2024.
2. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
3. Kohn DB, Hershfield MS, Puck JM, Aiuti A, Blincoe A, Gaspar HB, Notarangelo LD, Grunebaum E. Consensus approach for the management of severe combined immune deficiency caused by adenosine deaminase deficiency. *J Allergy Clin Immunol*. 2019 Mar;143(3):852-863.
4. Grunebaum E, Booth C, Cuvelier G, et al. Updated Management Guidelines for Adenosine Deaminase Deficiency. *J Allergy Clin Immunol Pract* 2023;11:1665-75.
5. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2024; Updated periodically.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.